An Introduction to Pragmatic Trials: A view into the rationale and process of real world interventions

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Colorado Pragmatic Research in Health Conference

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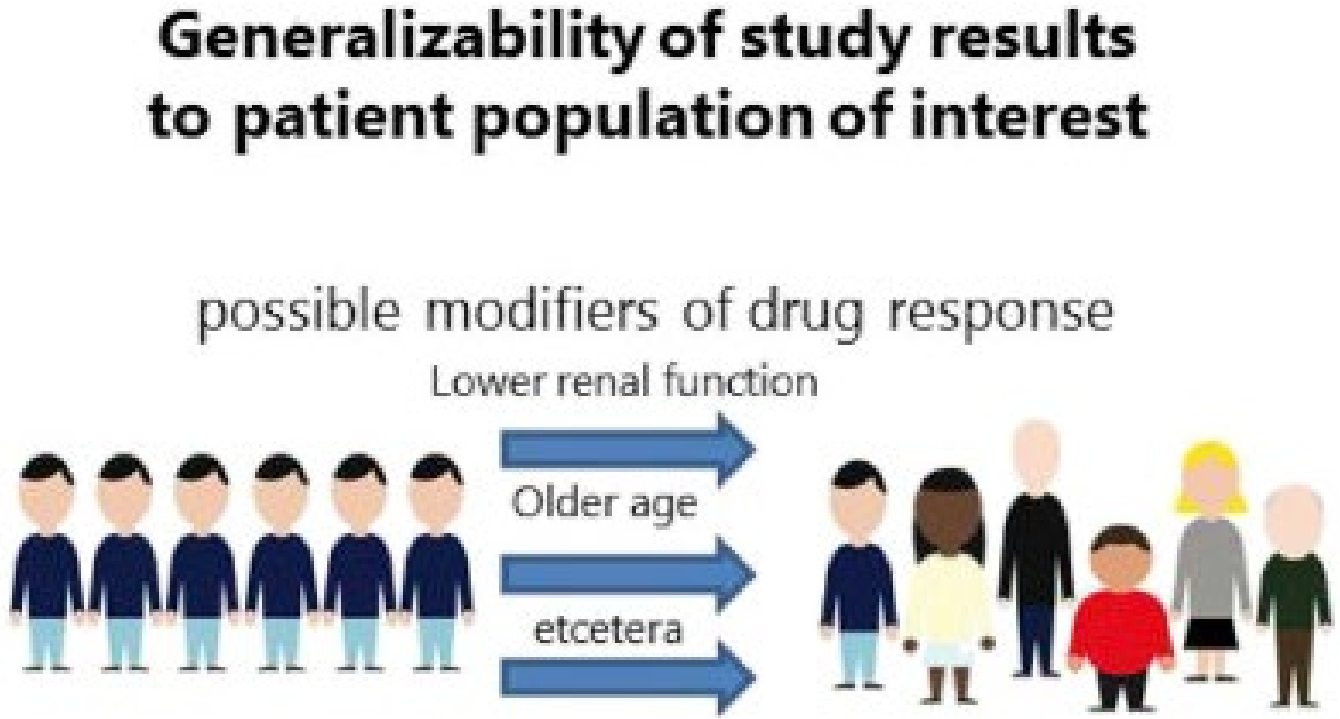
What is a pragmatic trial?

Pragmatic clinical trials seek to determine the effectiveness of an intervention in a real-world setting to inform clinical decision making - Roland and Torgerson 1998

Pragmatic trials are intended to help typical clinicians and typical patients make difficult decisions in typical clinical care settings by maximizing the chance that the trial results will apply to patients that are usually seen in practice (external validity). – Sox 2016

Pragmatic clinical studies aim to provide research results that better reflect everyday health care and a wider range of patients. Traditionally, clinical studies test how well treatments or other care approaches work under ideal conditions with carefully selected patients. - PCORI

What is a Pragmatic Trial?



Journal of Clinical Epidemiology 2017 887-13DOI: (10.1016/j.jclinepi.2016.12.023)

Cooking is like….

Efficacy Trial is Not Enough

- 1967: Schwartz D, Lellouch J. proposed that the efficacy (explanatory) trials are insufficient in that their goal is to:
  - Assess the efficacy of two interventions
  - Focus on the treatment working on the key clinical outcome of interest
  - Under a level of optimal administration

Aimed at understanding!

- The gap they proposed was:
  - Effect takes into account patient interest and the cost from a broad sense.
  - The patient population are extrapolated beyond the efficacy trial (all patients applicable)

Aimed at decision!

Why do we need pragmatic trials?

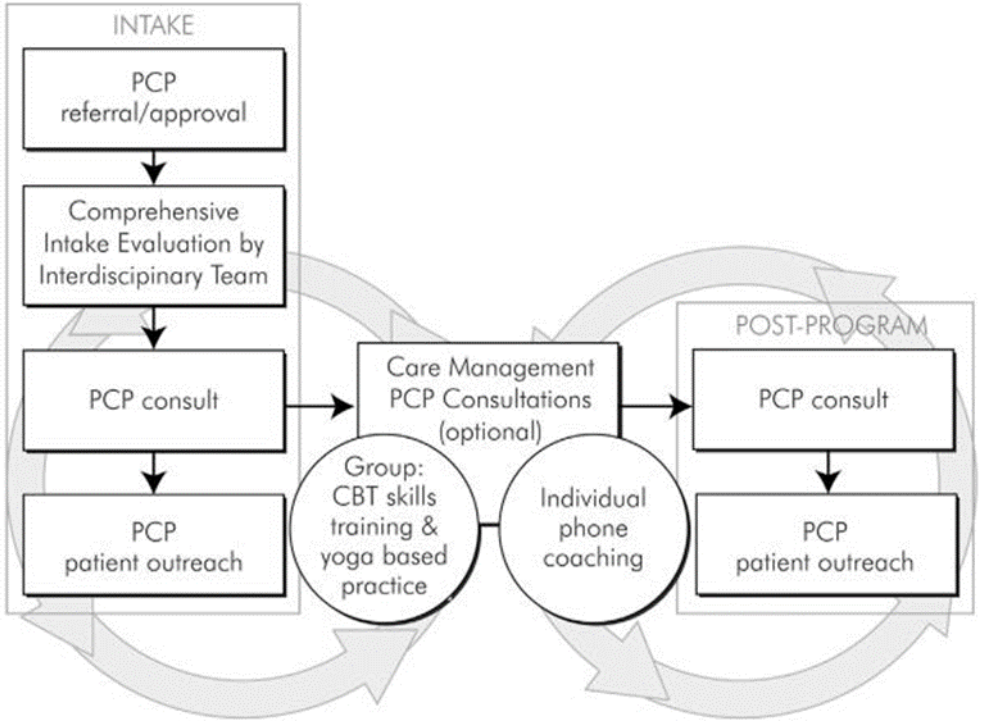
18,000+ randomized clinical trials published each year along with tens of thousands of other clinical studies. – Chalmers 2014

Systematic reviews consistently report not having enough evidence to effectively inform clinical decisions for providers and patients. – Patsopoulos 2011

"Between measurements based on RCTs and benefit … in the community there is a gulf which has been much under-estimated" - AL Cochrane, 1971

We can only do this as a pragmatic trial!

- Pain Program for Active Coping and Training (PPACT) – DeBar 2018
- “A variety of therapeutic modalities typically rely on teams of physicians, behavioral specialists, nurse case managers, and physical therapists to help patients develop skills to actively cope with and self-manage their condition”
- “The aim of our cluster-randomized pragmatic trial is to build on these studies by testing a program for its feasibility and sustainability within primary care to help patients adopt self-care and coping skills for managing chronic pain, limit use of opioid medications, and identify exacerbating factors amenable to treatment.”



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Designs

Trial Design

Things to do before you start	Efficacy Trial	Pragmatic Trial
Aim	√	
Hypothesis	√	
Power Calculation	√	
Eligibility Criteria	√	
Randomization	√	
Recruitment Strategy	√	
Data Capture Process	√	

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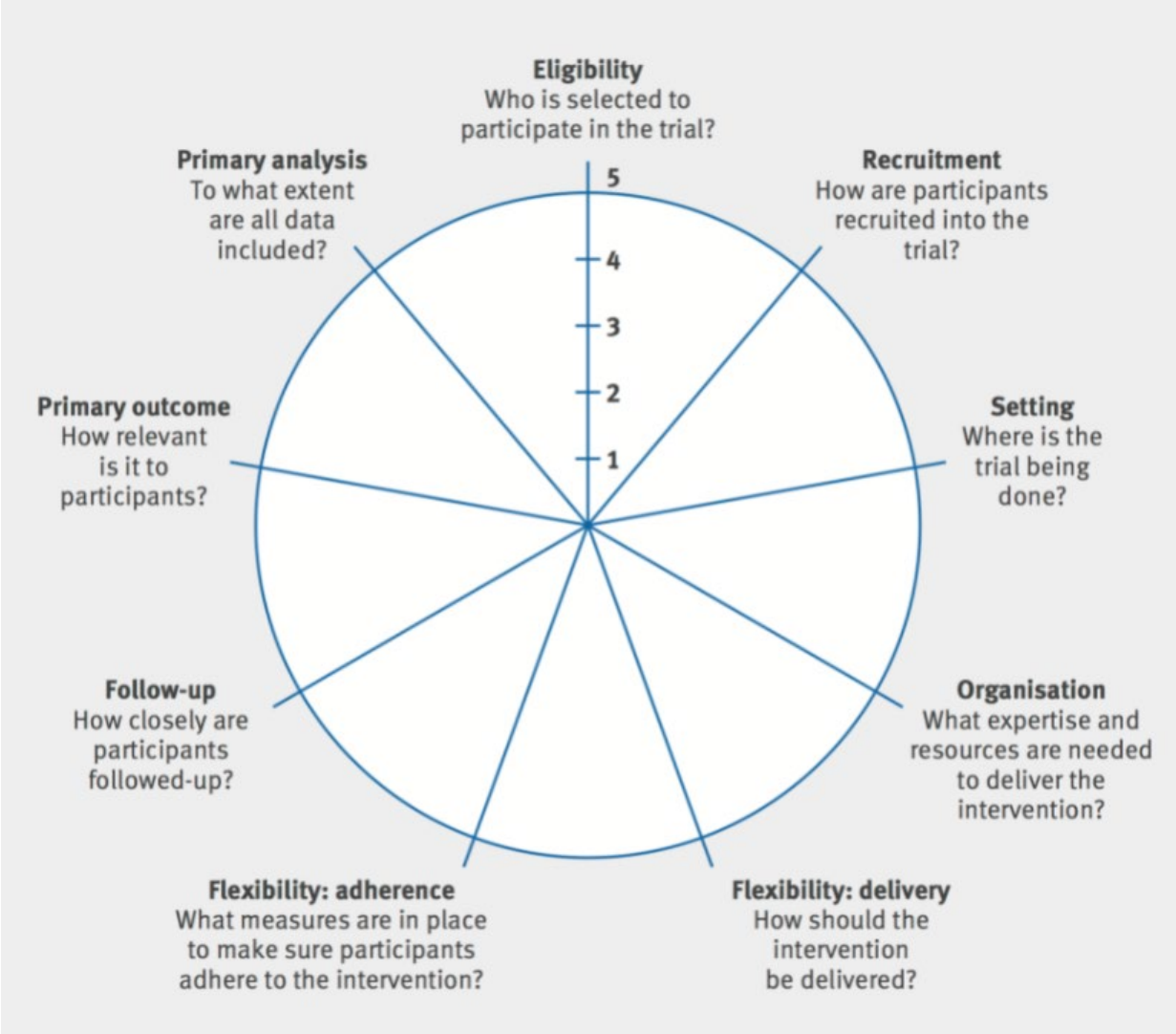

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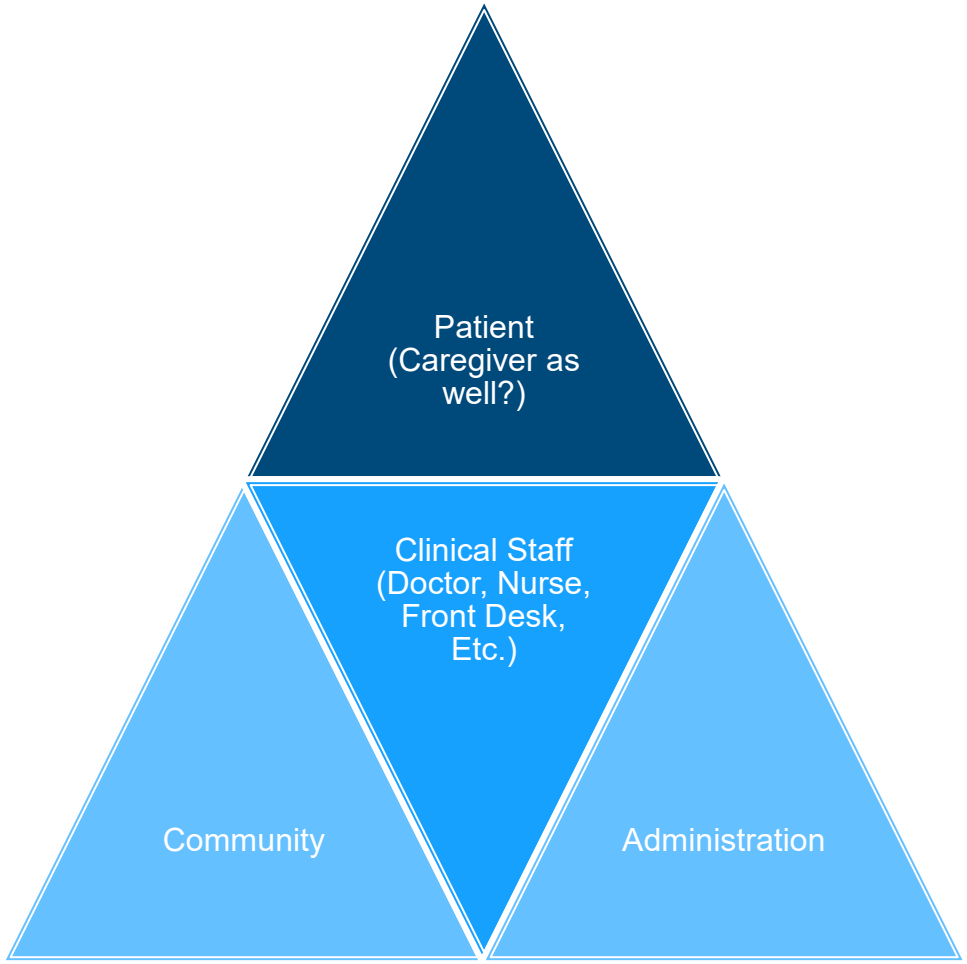
Approach

Outcomes: Whose needs/questions needs to be addressed?



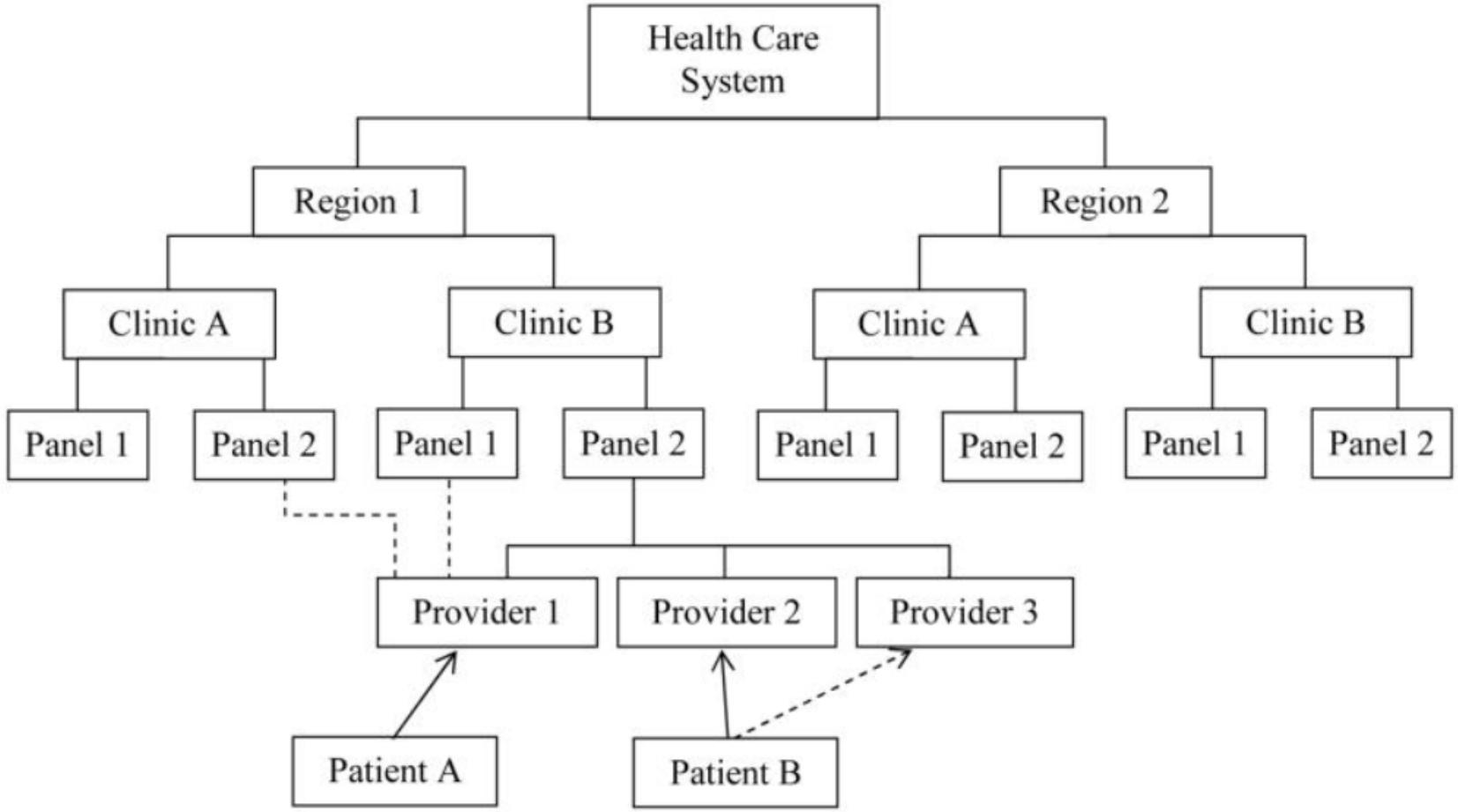
Who are the stakeholders?

The Patient Voice

- How they can help if we give them a chance!
  - SCOT Trial – Sullivan et al 2018
    - Patients with Scleroderma
    - Primary outcome: Event Free Survival
    - Recruitment: 75 (33% of Goal)
  - What was next?
    - Conducted focus groups with patients for input
    - Engaged a patient partner, a champion
    - Patients voiced preferences on outcomes of interest
    - Redesigned study and with input conducted study successfully with an N of 278
      - Patient Champion went on to speak at conferences and publish commentary on experience:

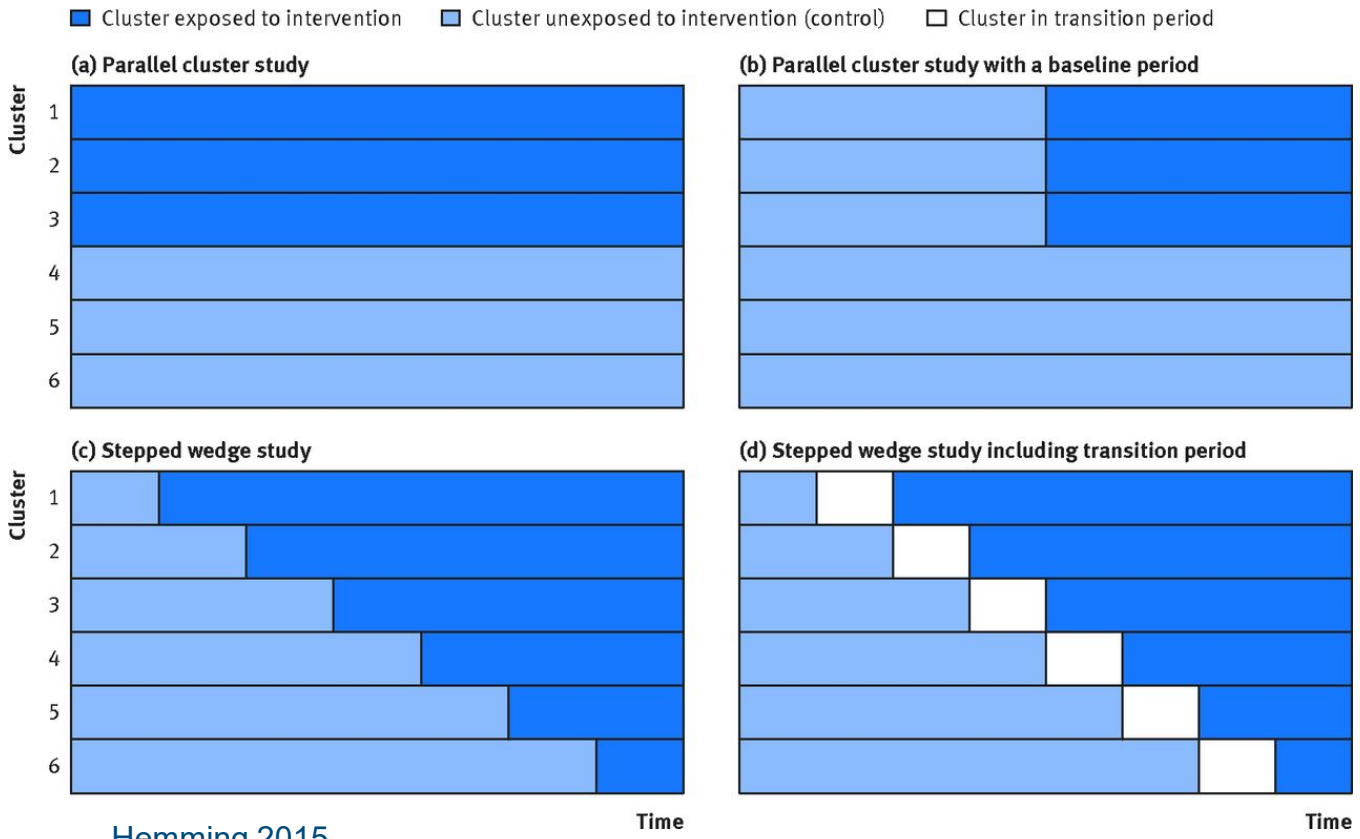
      Burch T. Patient Commentary: Added Value and Validity to Research Outcomes Through Thoughtful Multifaceted Patient-Oriented Research. Patient. 2020

Randomization

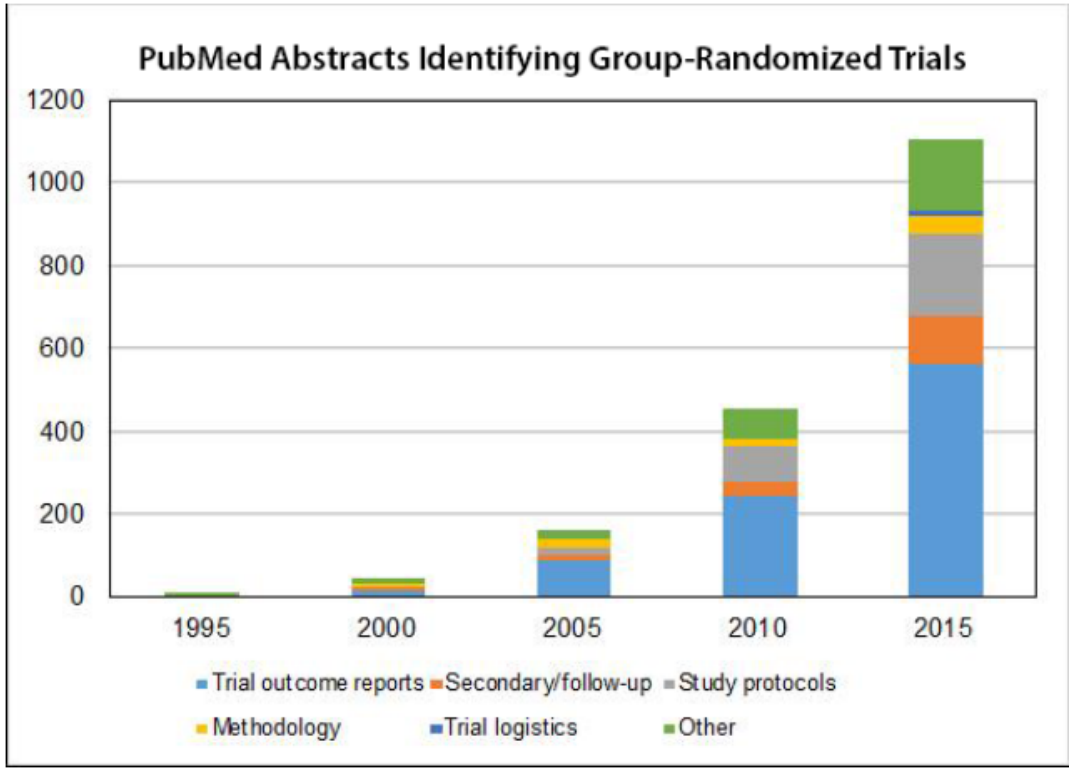


Cook et al 2016

Pragmatic is Mostly at Cluster!



Hemming 2015



NIH Group or Cluster Randomized Trials
https://researchmethodsresources.nih.gov/methods/grt

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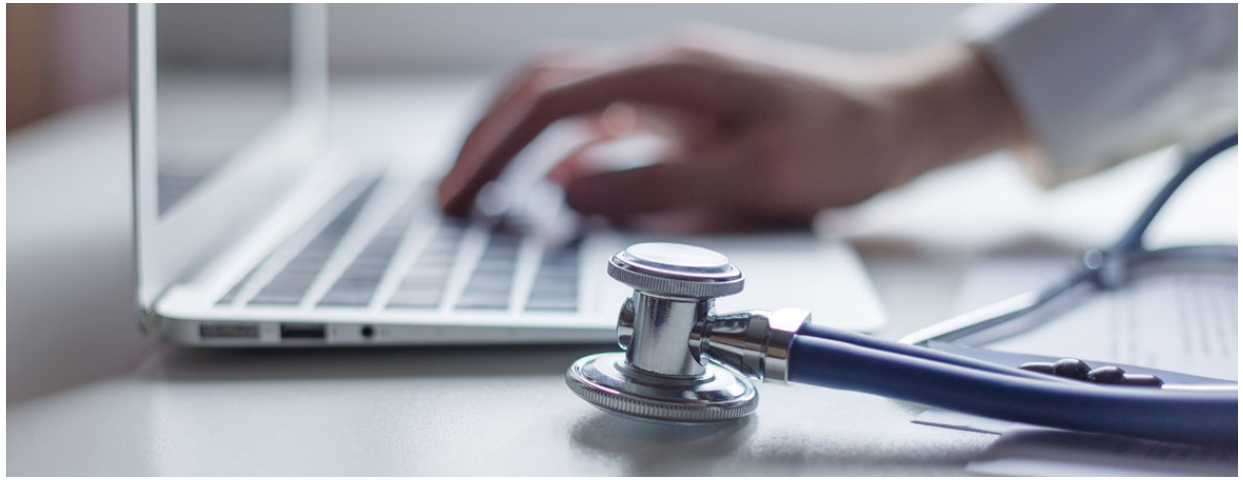
Leveraging Informatics

- Randomization
- Identifying patients
- Collecting utilization, clinical outcome and patient reported outcomes
- Contacting patients
- Enable access to intervention



Patient Identification - Challenges

- Standard recruitment strategies:
  - Clinician verification
  - Patient consent with confirmation of eligibility criteria

- Identification of cohorts within the EHR:
  - Under diagnosis
  - Improper diagnosis (miscode)
  - Missing data

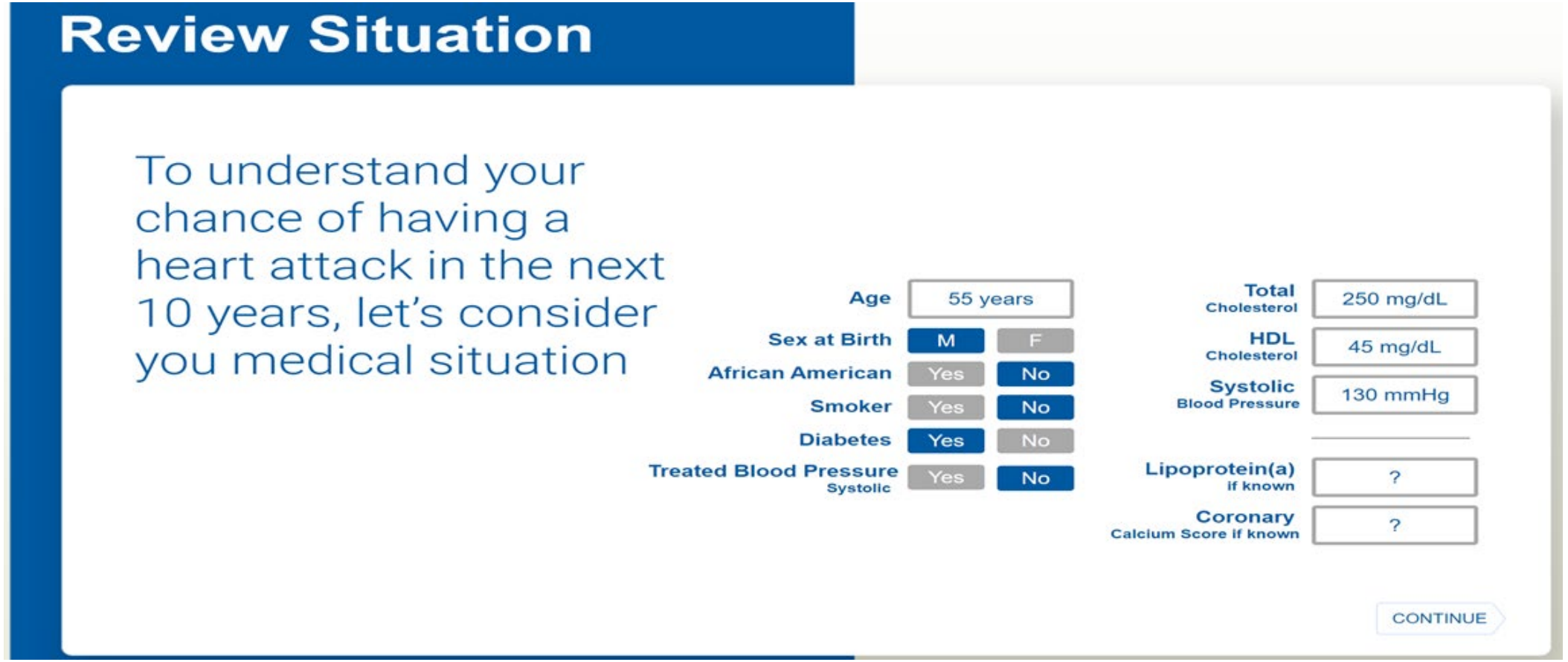
To address these issues phenotypes are being developed.

Recruitment

- ADAPTABLE Trial (Aspirin Dosing: A Patient-centric Trial Assessing Benefits and Long-Term Effectiveness) – Pfaff et al. 2019
  - 28% of patients enrolled in My Chart (EPIC™)
  - Did an experiment within the trial to assess most effective means for recruitment

Method	Type	Enrolled/Approached	% Enrolled
In clinic	Study Coordinator	57/339	17%
By e-mail	Electronic Recruitment	145/3891	4%
My Chart message	Electronic Recruitment	364/8363	4%
By mail	Paper	14/427	3.3%

CV Prevention Choice: SDMIP Pragmatic Trial



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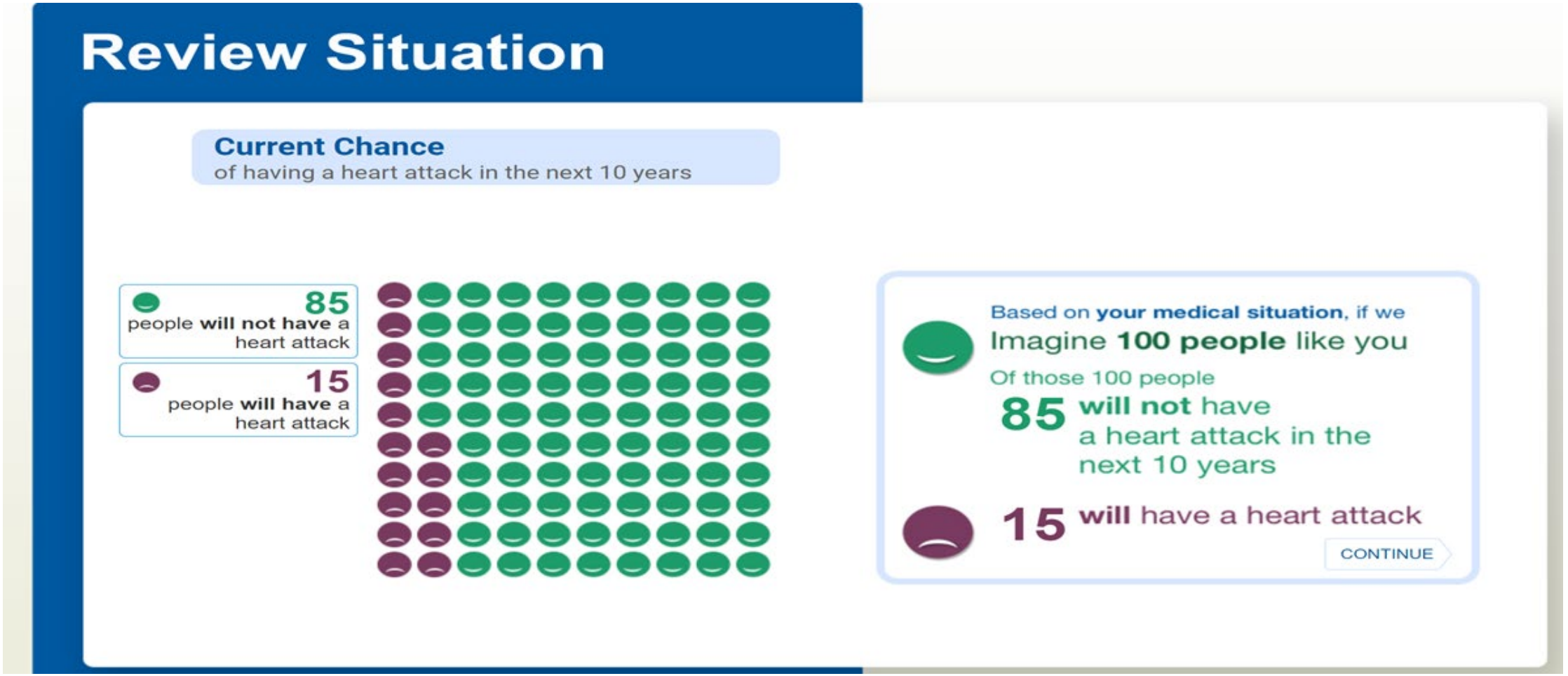
CV Prevention Choice: SDMIP Pragmatic Trial



Working with IT

Variables for abstraction and frequency

Data will be abstracted and transferred via secure FTP to Mayo Clinic within the first week of each month after the tool is initiated in the EHR.

Which Encounters will be abstracted and transferred:

- Encounters from participating practices only.
- Timeframe: Usual Care, active implementation and maintenance implementation
- Patient that meets eligibility criteria will be part of the abstraction
  - If a patient has multiple encounters, as long as the patient still meets eligibility criteria for that encounter then the encounter information will be transferred

Data to be transferred each time (one row per Encounter).

Data Item	Definition	Variable Name (Label for column being transferred)
Patient Identifier (random, unique)	Each patient will be assigned a random ID by the participating site. This site will keep a link between the random ID and the patients MRN till analysis is complete (end of year 4). If a patient has multiple encounters then the same ID will be used for each one.	Patient_id
Date of index visit	Date of the encounter (index visit)	Dt_visit
Clinician Identifier	Clinicians will be assigned a random identifier by the participating site. The site will keep the link between the clinician's name and the random identifier till analysis is complete (end of year 4).	Clinician_id
Age	Age of patient at time of encounter (integer)	Patient_age
Race	Patients race as a character string. Show each value recorded for Race (I.e. if the EHR has 5 Race field[illegible] report for each field).	Patient_race1 (if applicable: Patient_race2, Patient_race3, etc.)

In conclusion

- I have just touched on the concepts and items to consider…

- When thinking of designing a pragmatic trial
  - Consider the context of the setting and resources needed for the intervention!
  - Who are your stakeholders?
  - What footprint will your research have?
  - What resources can you leverage and what bias will they introduce?

Thank you!

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